In situ melanoma biomarker detection on a novel skin cancer 3D model via immunodiagnostic microneedles

S Totti [1], KW Ng[2], G Lian[1,3], T Chen[1], EG Velliou[1]

[1] *Bioprocess and Biochemical Engineering group (BioProChem), Department of Chemical and Process Engineering, University of Surrey, Guildford.* [2] *School of Pharmacy, Newcastle University, Newcastle upon Tyne.* [3] *Unilever R&D Colworth, Bedfordshire*

INTRODUCTION: Metastatic melanoma is the most lethal skin cancer. The prognosis for patients with distant metastasis is particularly poor and the 5-year survival rate is a dismal 20% [1]. To improve these disappointing statistical figures, it is essential to better understand the tumour's behaviour, progression and response and/or resistance to treatment options. Recent advances in tissue engineering enable the development of more physiologically relevant models that can recapitulate important features of the tumour tissue, i.e., the so-called tumour microenvironment (TME). More specifically, biomaterial based scaffolds can simulate important topological tissue features that affect the disease's progression and response to treatment, such as porosity, structure, extracellular matrix presence, cell-cell and cell-matrix interactions, environmental gradients and vascularization [2-4]. To date, the most effective treatment for melanoma is early diagnosis followed by surgical resection. Towards rapid diagnosis, minimally invasive microneedles are solid or hollow microstructures that enable rapid and pain-free biomarker detection *in situ* [5]. *The aim of this work was to develop and further validate the S100, a marker that is upregulated in melanoma, on a microporous polymer based 3D melanoma model. S100 expression in the model was confirmed using an immunodiagnostic microneedle device.*

METHODS: The overall procedure followed is depicted in Figure 1. 3D polymer (PU) based microporous scaffolds were developed and the metastatic melanoma cell line A-375 was injected and cultivated in those scaffolds for 5 weeks. Quantitative assessment of cell viability took place with the MTS metabolic assay and evaluation of cell distribution within the PU matrix was conducted with Scanning Electron Microscopy (SEM). Viable (live) cells were visualised *in situ* with confocal laser scanning microscopy (CLSM) of several sections of each scaffold. Furthermore, the detection of the S100 melanoma specific marker was carried out with microneedles via immunoassay analysis on their surface.

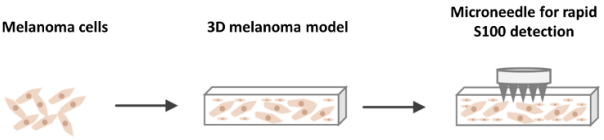

Fig 1. Developed platform for S100 detection in the 3D melanoma model.

RESULTS: The 3D microporous scaffolds were able to support the long term cultivation of the A-375 cells, with the majority of them being viable until the culture endpoint. Dense melanoma cell masses adhered to the scaffold pores and were distributed throughout the 3D matrix. Additionally S100 detection was achieved via immunodiagnostic microneedle administration on the surface of the 3D scaffolds.

DISCUSSION & CONCLUSIONS: Our findings indicate that this 3D polymer based microporous system is a promising tool for *ex vivo* modelling of metastatic melanoma. Furthermore, to our knowledge, this is the first time that a 3D *in vitro* melanoma model is used for validation of biomarker detection with microneedles. Our findings suggest that this 3D microporous melanoma scaffold can be used as a low cost tool for validation/screening of novel cancer detection methods and/or kits, replacing and/or reducing animal testing for the validation of such kits.

REFERENCES: [1] R.L. Siegel, K.D. Miller, and A. Jemal. (2018) *CA Cancer J Clin* **68**:7-30. [2] S. Totti, S.I. Vernardis, L. Meira, et al (2017) *Drug Discov Today* **22**, 690-701. [3] S. Totti, M. Allenby, S B. Dos Santos, et al (2017) *Eur Cells Mater* **33** (Suppl. 2), 0249, [4] S. Totti, S B. Dos Santos, M. Allenby, et al (2016) *Eur Cells Mater* **31**(Suppl. 1), P441**,** [5] K.W. Ng, W.M. Lau, and A.C. Williams (2015) Drug Deliv and Transl Res **5**, 387-96.

ACKNOWLEDGEMENTS: This work was supported by University of Surrey as well as an Impact Acceleration Grant (IAA-KN9149C) of the University of Surrey, an IAA –EPSRC Grant (RN0281J) and the Royal Society.